Regio- and stereoselective 1,3-Oxathiolane formation in the reaction of Thiolactones with optically active oxiranes

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Abstract: The reactions of 3H-isobenzofuran-1-thione (1) with (S)-2-methyloxirane (2) and (R)-2-phenyloxirane (6) in the presence of SiO2 in anhydrous CH2Cl2 led to two pairs of diastereoisomeric spirocyclic 1,3-oxathiolanes, i.e., 3 and 4 with a Me group at C(5'), and 7 and 8 with a Ph group at C(4'), respectively (Schemes 2 and 3). In both cases, 3H-isobenzofuran-1-one (5) was formed as a main product. The analogous reactions of 3,4-dihydro-2H-[1]benzopyran-2-thione (9) and 3,4,5,6-tetrahydro-2H-pyran-2-thione (14) with 2 and 6 yielded four pairs of the corresponding diastereoisomeric spirocyclic compounds 10 and 11, 12 and 13, 15 and 16, and 18 and 19, respectively (Schemes 4 - 7). In the reaction of 14 with 6, the 1,3-oxathiolane 20 with a Ph group at C(2) was also formed. The structures of 3, 7, 8, 10, 19, and 20 were established by X-ray crystallography (Figs.1-4). In contrast to the thiolactones 1, 9, and 14, the thioesters 21a-21d did not react with (R)-2-phenyloxirane (6) either in the presence of SiO2 or under more-drastic conditions with BF3 . Et2O or SnCl4 (Scheme 8). The results show that spirocyclic 1,3-oxathiolanes can be prepared from thiolactones with oxiranes. The nucleophilic attack of the thiocarbonyl S-atom at the SiO2-activated oxirane ring proceeds with high regio- and stereoselectivity via an SN2-type mechanism.

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Regio- and Stereoselective 1,3-Oxathiolane Formation in the Reaction of Thiolactones with Optically Active Oxiranes

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[1]) Part IV of the projected Ph.D. thesis of *C. F.*, University of Zurich. Part I: see [1], Part II: see [2], Part III: see [3].

The reactions of 3*H*-isobenzofuran-1-thione (**1**) with (*S*)-2-methyloxirane (**2**) and (*R*)-2-phenyloxirane (**6**) in the presence of SiO_2 in anhydrous CH_2Cl_2 led to two pairs of diastereoisomeric spirocyclic 1,3-oxathiolanes, *i.e.*, **3** and **4** with Me at C(5′), and **7** and **8** with Ph at C(4′), respectively (*Schemes 2 – 3*). In both cases, 3*H*-isobenzofuran-1-one (**5**) was formed as a main product. The analogous reactions of chroman-2-thione (**9**) and tetrahydropyran-2-thione (**14**) with **2** and **6** yielded four pairs of the corresponding diastereoisomeric spirocyclic compounds **10** and **11**, **12** and **13**, **15** and **16**, and **18** and **19**, respectively (*Schemes 4 – 7*). In the reaction of **14** with **6**, the 1,3-oxathiolane **20** with Ph at C(2) was also formed. The structures of **3**, **7**, **8**, **10**, **19**, and **20** were confirmed by X-ray crystallography (*Figs. 1 – 4*). In contrast to the thiolactones **1**, **9**, and **14**, the thioesters **21a** – **d** did not react with (*R*)-2-phenyloxirane (**6**) either in the presence of SiO_2 or under more drastic conditions with $BF_3{\cdot}Et_2O$ or $SnCl_4$ (*Scheme 8*). The results show that spirocyclic 1,3-oxathiolanes can be prepared from thiolactones with oxiranes. The nucleophilic attack of the thiocarbonyl S-atom at the SiO_2-activated oxirane ring proceeds with high regio- and stereoselectivity *via* an S_N2-type mechanism.

1. Introduction. – The formation of 1,3-oxathiolanes *via* the *Lewis* acid-catalyzed reaction of thioketones with oxiranes has been investigated thoroughly in recent years [1 – 6]. The reported results for this novel synthetic approach indicate that the reactions proceed with high regio- and stereoselectivity *via* an S_N2-type mechanism (*Scheme 1*). In the case of 2-alkyl-substituted oxiranes, the nucleophilic thiocarbonyl S-atom attacks preferentially at C(3) to give the 5-substituted 1,3-oxathiolanes with retention of the configuration at C(2) of the oxirane. On the other hand, 2-phenyloxirane is attacked mainly at C(2) under inversion of the configuration to yield the 4-phenyl-substituted products. Similar reactions have been observed with 1,3-thiazole-5(4*H*)-thiones [7] [8], with cyclic trithiocarbonates [9], and with a rhodanine derivative [10].

Scheme 1

So far, the reaction of thioesters with oxiranes to afford 1,3-oxathiolanes, *i.e.*, monothioorthoesters, has not been reported. With the aim of further extending the scope of the formation of 1,3-oxathiolanes, reactions of thiolactones such as 3*H*-isobenzofuran-1-thione (**1**), chroman-2-thione (**9**), tetrahydropyran-2-thione (**14**), as well as of thioesters, *i.e.*, *O*-ethyl 2,2-dimethylthiopropanoate (**21a**), *O*-methyl thiooctanoate (**21b**), *O*-methyl thiobezoate (**21c**), and *O*-phenyl thiobenzoate (**21d**), with optically active oxiranes were carried out. In the present paper, the results of the reactions of **1**, **9**, and **14** with (*S*)-2-methyloxirane (**2**) and (*R*)-2-phenyloxirane (**6**), and those of **21a** – **d** with **6** are described.

2. Results. – 2.1. *Reaction of 3*H*-Isobenzofuran-1-thione* (**1**) *with (*S*)-2-Methyloxirane* (**2**). The reaction of **1** with **2** in a molar ratio of 1:2 was carried out in anhydrous CH_2Cl_2 at room temperature under an N_2 atmosphere in the presence of SiO_2. After stirring for 10 h, filtration and the usual workup by means of

column chromatography (CC) and HPLC on a chiral solid phase gave two diastereoisomeric spirocyclic 1,3-oxathiolanes **3** and **4** in 16 and 8% yield, respectively. The reaction was repeated under the same conditions, and the analysis of the reaction mixture by ^{1}H-NMR spectroscopy showed 26% of **3**, 10% of **4**, as well as 54% of 3*H*-isobenzofuran-1-one (**5**) and 9% of **1**, referenced to a weighed amount of 1,1,2,2-tetrachloroethane as a standard (*Scheme 2*). The enantiomeric excess (ee) of the products (> 99%) was determined by analytical HPLC (*Chiralcel OD-H*, hexane/i-PrOH 25:1).

Scheme 2

The structures of **3** and **4** were assigned on the basis of the elemental analyses, MS, IR, ^{1}H- and ^{13}C-NMR (2D-NOESY, HSQC, HSQC-TOCSY, and HMBC) spectra, which clearly indicated the relative configurations of the products. The 2D-NOESY spectrum of **3** showed one cross-signal between H–C(7) at 7.51–7.50 ppm and Me at 1.48 ppm, and that of **4** gave one cross-signal between H–C(7) at 7.49–7.48 ppm and H–C(5′) at 4.70–4.67 ppm. The formation of **3** and **4** proceeded by nucleophilic attack of the thiocarbonyl S-atom at C(3) and, for this reason, the configuration at C(2) of the oxirane **2** is retained. Therefore, the configuration at C(1) in **3** and **4** should be 1*R* and 1*S*, respectively, relative to the known 5′*S*-configuration[2]). Finally, the structure of **3** was established by X-ray crystallography (*Fig. 1*).

Fig. 1

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[2]) This proposal was proven by the X-ray crystal-structure analysis of **10** (see *Sect. 2.3*).

The crystals of **3** were enantiomerically pure, but due to the quality of the crystals, the absolute configuration of the molecule could not be confirmed unequivocally by refinement of the absolute structure parameter. The enantiomer used in the refinement was therefore chosen to correspond with the known 5′*S*-configuration. Based on this assumption, the stereogenic centre at C(1) has the *R*-configuration.

2.2. *Reaction of 3*H-*Isobenzofuran-1-thione* (**1**) *with (*R*)-2-Phenyloxirane* (**6**). The analogous reaction of **1** with **6** (molar ratio 1:1.5) in anhydrous CH_2Cl_2 at room temperature for 10 h under an N_2 atmosphere in the presence of SiO_2 gave two diastereoisomeric spiroheterocycles **7** and **8** in 29 and 10% yield, respectively. The repetition of the reaction led to **7**, **8**, **5**, and **1** in 29, 16, 29, and 26% yield, respectively, based on the ^{1}H-NMR spectrum of the reaction mixture and 1,1,2,2-tetrachloroethane as an internal standard (*Scheme 3*). The ee values of the products (> 99%) were determined by analytical HPLC (*Chiralcel OD-H*, hexane/i-PrOH 25:1). It was to be expected that **7** and **8** were formed *via* the nucleophilic attack of the S-atom at C(2) of **6** with inversion of the configuration, leading to the *S*-configuration at C(4′) of the products.

Scheme 3

The structures of **7** and **8** were assigned on the basis of their elemental analyses and spectroscopic data, particularly 2D-NOESY, HSQC, HSQC-TOCSY, and HMBC NMR spectra, and they were confirmed by X-ray crystallography (*Fig. 2*). The 2D-NOESY spectrum of **7** showed no significant cross-signals which could be used for the determination of the relative configuration, but that of **8** gave one weak cross-signal between two *ortho*-H atoms of Ph at 7.59–7.58 ppm and two H–C(3) at 5.23–5.17 ppm, which indicated that **8** has the *cis*-configuration, *i.e.*, the 1*R*,4′*S*-configuration. Therefore, the diastereoisomer **7** should have the

1*S*,4′*S*-configuration, which is in accordance with the X-ray crystal-structure analysis.

Fig. 2

The crystals of **7** and **8** were enantiomerically pure and the absolute configurations of the molecules have been determined independently by the diffraction experiment and found to have the 1*S*,4′*S*- and 1*R*,4′*S*-configuration, respectively.

2.3. *Reaction of Chroman-2-thione* (**9**) *with (*S*)-2-Methyloxirane* (**2**). The reaction of **9** with **2** in a molar ratio of 1:2 was carried out in anhydrous CH_2Cl_2 at room temperature under an N_2 atmosphere in the presence of SiO_2. After stirring for 3 d, filtration and the usual workup by means of column chromatography (CC) gave a 4:1 mixture (^{1}H-NMR) of two diastereoisomeric spirocyclic 1,3-oxathiolanes **10** and **11** in 40% total yield (*Scheme 4*). Separation of the mixture by HPLC led to **10** in 29% yield, but **11** could not be obtained in pure form because of its partial epimerization to **10**. The ee of **10** (> 99%) was determined by analytical HPLC (*Chiralcel OD-H*, hexane/i-PrOH 50:1).

Scheme 4

The structure of **10** was again assigned on the basis of the elemental analysis and the spectroscopic data, particularly those obtained from NMR experiments. The 2D-NOESY spectrum of **10** showed one cross-signal between H–C(8) at 6.83 ppm and H–C(5′) at 4.83–4.78 ppm, which clearly indicated the *S*-configuration at C(2) relative to the known 5′*S*-configuration. Therefore, the diastereoisomer **11**, should have the 2*R*,5′*S*-configuration. Finally, the structure of **10** was established by X-ray crystallography (*Fig. 3*).

Fig. 3

The crystals of **10** were enantiomerically pure and the absolute configuration of the molecule has been determined independently by the diffraction experiment: the molecule has the expected 2*S*,5′*S* configuration.

2.4. *Reaction of Chroman-2-thione* (**9**) *with (*R*)-2-Phenyloxirane* (**6**). The analogous reaction of **9** with **6** (molar ratio 1:1.5) in anhydrous CH_2Cl_2 at room temperature for 3 d under an N_2 atmosphere in the presence of SiO_2 gave two diastereoisomeric spirocyclic compounds **12** and **13** in 35 and 7% yield, respectively. The ee values of the products, determined by analytical HPLC (*Chiralcel OD-H*, hexane/i-PrOH 50:1), showed that **12** and **13** were formed with lower stereoselectivity, and partial racemization of *ca.* 10% was observed (*Scheme 5*).

Scheme 5

The structures of **12** and **13** were assigned in the same way as that of **10**. According to previous reactions of thiocarbonyl compounds with **6**, the formation of **12** and **13** was expected to take place mainly *via* inversion of the configuration at C(2) of **6**, which leads to the 4′*S*-configuration of the products. The 2D-NOESY spectrum of **12** showed two cross-signals between two *ortho*-H atoms of Ph at 7.40–7.39 ppm and two H–C(3) at 2.60–2.55 and 2.51–2.46 ppm, respectively, which indicated the 2*R*,4′*S*-configuration. On the other hand, the 2D-NOESY spectrum of **13** showed one cross-signal between two *ortho*-H atoms of Ph at 7.53 ppm and H–C(8) at 6.95–6.93 ppm, and another one between H–C(4′) at 4.94 ppm and two H–C(3) at 2.51–2.40 ppm indicating the 2*S*,4*S*-configuration.

2.5. *Reaction of Tetrahydropyran-2-thione* (**14**) *with (*S*)-2-Methyloxirane* (**2**). The reaction of **14** with **2** (molar ratio 1:2) in anhydrous CH_2Cl_2 at 0°C for 2 d under an N_2 atmosphere in the presence of SiO_2 gave two diastereoisomeric spirocyclic 1,3-oxathiolanes **15**, **16**, together with lactone **17** in 63, 22, and 15% yield, respectively, based on the ^{1}H-NMR spectrum of the reaction mixture and 1,1,2,2-tetrachloroethane as a standard (*Scheme 6*). Separation of the two diastereoisomers by MPLC and HPLC gave **15** as a pure compound in 38% yield, but **16** was obtained only in 90% purity because of its partial epimerization to **15**. The ee value of **15** was determined by analytical HPLC as > 99% (*Chiralcel OB*, hexane/EtOH 80:1).

Scheme 6

As in the previous cases, the structures of **15** and **16** were assigned on the basis of their elemental analysis and spectroscopic data. The 2D-NOESY spectrum of **15** showed one cross-signal between H–C(2) at 4.65–4.59 ppm and one H–C(7) at 3.94–3.90 ppm, which indicated the *trans*-configuration, *i.e.*, the *R*-configuration at C(5) relative to the known 2*S*-configuration. On the other hand, the spectrum of **16** showed one cross-signal between H–C(2) at 4.33–4.28 ppm and two H–C(10) at 2.11–2.01 ppm, which implies the 2*S*,5*S*-configuration.

2.6. *Reaction of Tetrahydropyran-2-thione* (**14**) *with (*R*)-2-Phenyloxirane* (**6**). The analogous reaction of **14** with **6** (molar ratio 1:1.5) in anhydrous CH_2Cl_2 at room temperature for 11 h under an N_2 atmosphere in the presence of SiO_2 gave three spirocyclic 1,3-oxathiolanes **18**, **19**, and **20** in 54, 11, and 8% yield, respectively. The ee values of the products, determined by analytical HPLC (*Chiralcel OB*, hexane/EtOH 80:1), showed that the reaction proceeded with lower stereoselectivity and partial racemization (10% in the case of **19**) (*Scheme 7*).

Scheme 7

The structures of **18**, **19**, and **20** were assigned as usual. The 2D-NOESY spectrum of **18** showed one cross-signal between two *ortho*-H atoms at 7.38–7.36 ppm and two H–C(10) at 2.27–2.16 ppm, indicating the *trans* (3*S*,5*S*)-configuration. The 1D-NOESY spectrum of **19**, on irradiation of H–C(3) at 4.8 ppm, gave one NOE-signal for two H–C(10) at 2.17–2.05 ppm, corresponding to the *cis* (3*S*,5*R*)-configuration. Finally, the 2D-NOESY spectrum of **20** showed one cross-signal between two *ortho*-H atoms of Ph at 7.47–7.45 ppm and one H–C(7) at 4.06–4.02 ppm, and another one between H–C(2) at 5.30 ppm and two H–C(10) at 2.17–2.08 ppm, indicating the 2*R*,5*R*-configuration. The structures and absolute configurations of **19** and **20** were established by X-ray crystallography (*Fig. 4*).

Fig. 4

The crystals of **19** and **20** were enantiomerically pure and the absolute configurations of the molecules have been determined independently by the diffraction experiment. The molecules of **19** and **20** have the 3*S*,5*R*- and 2*R*,5*R*-configuration, respectively.

2.7. *Reactions of Thioesters* **21a** – **d** *with (*R*)-2-Phenyloxirane* (**6**). In analogy to the reactions with thiolactones (*Sect. 2.1 – 2.6*), the reactions of **21a** – **d** with **6** were carried out in anhydrous CH_2Cl_2 at room temperature for 2 – 6 d under an N_2 atmosphere in the presence of SiO_2. Surprisingly, none of the expected 1,3-oxathiolanes was formed. Therefore, the reactions of **21a** – **b** with **6** were repeated in anhydrous CH_2Cl_2 at – 78° for 20 – 30 min under an N_2 atmosphere in the presence of the stronger *Lewis* acids $BF_3{\cdot}Et_2O$ or $SnCl_4$, but they did not lead to any of the expected product, either (*Scheme 8*).

Scheme 8

3. Discussion and Conclusions. – The presented results show that thiolactones **1**, **9**, and **14** react with the monosubstituted oxiranes **2** and **6** to yield the spirocyclic 1,3-oxathiolanes with high regio- and stereoselectivity. On the other hand, no reactions occur between the thioesters **21a** – **d** with **6**. An S_N2-type mechanism for the 1,3-oxathiolane formation is proposed in *Scheme 9*, whereby the nucleophilic thiocarbonyl S-atom favorably attacks the C(3)-atom (O–C(3) cleavage) of the activated (*S*)-2-methyloxirane (**2**) to give the thiocarbonylium ion **A** with retention of the configuration. The latter undergoes ring closure by nucleophilic addition of the O-atom from the *si*- and *re*-face of the thiocarbonylium group to yield the spirocyclic 1,3-oxathiolanes **15** and **16**, respectively. On the other hand, the addition to (*R*)-2-phenyloxirane (**6**) occurs selectively at the C(2)-atom (O–C(2) cleavage) with inversion of the configuration leading to intermediate **B**. Cyclization of **B** by addition of the O-atom from the *re*- and *si*-face gives **18** and **19**, respectively. The partial loss of the stereochemical integrity of the phenyloxirane moiety in the formation of **19** may be interpreted by a competing reaction in which the oxirane ring-opening take place prior to the nucleophilic attack (S_N1-type). The formation of lactones in the cases of **1** and **14** can be explained by the hydrolysis of intermediates of type **A** and **B**.

Scheme 9

Although thiolactones **9** and **14** are enolizable, their reactions with oxiranes **2** and **6** do not yield the open-chain enesulfanyl alcohols apart from the spirocyclic 1,3-oxathiolanes, in contrast to the reactions of thiocamphor with oxiranes [2].

The observed epimerizations of **11** and **16** to the thermodynamically more stable epimers **10** and **15**, respectively, proceed smoothly during column

chromatography on SiO_2. This isomerization can be explained *via* acid-catalyzed ring opening of 1,3-oxathiolanes, as has been described in *Scheme 9* of [2].

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Experimental Part

1. *General*. See [12]. Optical rotations: *Perkin-Elmer-241* polarimeter (c = 1, in THF). IR spectra: film or KBr, cm^{-1}. NMR spectra at 600 (^1H) and 150.9 MHz (^{13}C) in $CDCl_3$. Enantiomeric excesses were determined by analytical HPLC on a *Chiralcel OD-H* or *Chiralcel OB* column. The thiolactones **1** [13], **9** [14], and **14** [15] have been prepared by thionation of the corresponding lactones following described procedures. Similarly, the thioesters **21a** – **d** were obtained from the esters by treatment with *Lawesson*'s reagent [16].

2. *General Procedure for the Reactions of 3*H-*Isobenzofuran-1-thione* (**1**)*, Chroman-2-thione* (**9**), *and Tetrahydropyran-2-thione* (**14**) *with (*S*)-Methyl- and (*R*)-Phenyloxirane* (**2** *and* **6**). To the soln. of **1**, **9**, or **14** (*ca.* 1 mmol) and oxirane **2** or **6** (*ca.* 2 mmol) in anh. CH_2Cl_2 (15 ml) under an N_2 atmosphere, 4.5 g of silica gel (SiO_2, *Uetikon-Chemie Chromatographiegel C-560*) were added at r.t. or 0°. After stirring the suspension for 10 h – 3 d at r.t. or 0°, the mixture was filtered and the residue was washed with Et_2O (4×). Then, the combined filtrate was evaporated *in vacuo.* and the products were separated by chromatography (SiO_2 or Alox; hexane/Et_2O, or hexane/AcOEt; CC, MPLC or HPLC).

3. *Reactions of* **1**. 3.1. *With (*S*)-2-Methyloxirane* (**2**). Reaction of **1** (300 mg, 2 mmol) with **2** (232 mg, 4 mmol) and 4.5 g of SiO_2 at r.t., 34 h, and CC (Alox,

hexane/Et_2O 10:1) yielded 115 mg (28%) of a mixture of *(1*R*,5′*S*)-5′-methylspiro[1,3-dihydroisobenzofuran-1,2′-[1,3]oxathiolane]* (**3**) and *(1*S*,5′*S*)-5′-methylspiro[1,3-dihydroisobenzofuran-1,2′-[1,3]oxathiolane]* (**4**). Separation of the two diastereoisomers by HPLC (*Chiralcel OD* column, hexane/i-PrOH 25:1) gave 68 mg (16%) of **3** and 35 mg (8%) of **4**. Repetition of the reaction of **1** (150 mg, 1 mmol) with **2** (116 mg, 2 mmol) for 10 h yielded 26% of **3**, 10% of **4**, and 54% of *3*H-*isobenzofuran-1-one* (**5**) based on ^{1}H-NMR analysis of the reaction mixture and a weighed amount of 1,1,2,2-tetrachloroethane as a standard. In addition, 9% of **1** remained (*Scheme 2*).

Data of **3**: Colorless crystals. M.p. 64.4 – 65.1 . $[\alpha]_D^{23}$ = + 136.4 (> 99% ee). IR (KBr): 3081*w*, 3049*w*, 3022*w*, 2975*m*, 2936*m*, 2915*m*, 2904*m*, 2864*m*, 1643*w*, 1476*w*, 1461*m*, 1450*w*, 1385*w*, 1358*w*, 1349*m*, 1281*m*, 1253*s*, 1227*w*, 1193*w*, 1182*w*, 1170*w*, 1140*m*, 1110*m*, 1088*m*, 1037*s*, 1009*s*, 998*s*, 962*m*, 951*s*, 937*s*, 912*m*, 852*m*, 768*s*, 732*w*, 713*w*. ^{1}H-NMR: 7.51–7.50 (*m*, H–C(7)); 7.38–7.36 (*m*, H–C(5), H–C(6)); 7.23–7.21 (*m*, H–C(4)); 5.15 (*d*, *J* = 12.6, 1 H–C(3)); 5.09 (*d*, *J* = 12.6, 1 H–C(3)); 4.67–4.64 (*m*, H–C(5′)); 3.36 (*dd*, *J* = 10.0, 4.7, 1 H–C(4′)); 3.03 (*t*, *J* = 10.1, 1 H–C(4′)); 1.48 (*d*, *J* = 6.1, Me). ^{13}C-NMR: 139.4 (*s*, C(3a)); 138.1 (*s*, C(7a)); 128.8 (*d*, C(5)); 128.3 (*d*, C(6)); 124.1 (*d*, C(7)); 124.0 (*s*, C(1)); 121.0 (*d*, C(4)); 78.9 (*d*, C(5′)); 72.0 (*t*, C(3)); 41.6 (*t*, C(4′)); 19.1 (*q*, Me). ESI-MS (MeOH + NaI): 439 (5, $[2M+Na]^+$), 231 (100, $[M + Na]^+$), 157 (45). Anal. calc. for $C_{11}H_{12}O_2S$ (208.28): C 63.43, H 5.81, S 15.40; found: C 63.35, H 5.86, S 15.40.

Crystals of **3** suitable for the X-ray crystal-structure determination were grown from hexane/i-PrOH.

Data of **4**: Colorless oil. $[\alpha]_D^{23}$ = – 63.7 (> 99% ee). IR (film): 3078*w*, 3039*w*, 2976*m*, 2930*m*, 2868*m*, 1612*w*, 1463*m*, 1437*w*, 1378*m*, 1353*m*, 1307*w*, 1281*m*, 1251*s*, 1198*w*, 1176*w*, 1140*w*, 1113*s*, 1088*m*, 1036*s*, 1025*s*, 1012*s*, 955*s*, 941*s*, 924*s*, 757*s*, 720*m*, 711*w*. ^{1}H-NMR: 7.49–7.48 (*m*, H–C(7)); 7.37–7.35 (*m*,

H–C(5), H–C(6)); 7.23–7.21 (*m*, H–C(4)); 5.20 (*d*, *J* = 12.6, 1 H–C(3)); 5.05 (*d*, *J* = 12.6, 1 H–C(3)); 4.70–4.67 (*m*, H–C(5′)); 3.35 (*dd*, *J* = 10.6, 5.2, 1 H–C(4′)); 3.17 (*dd*, *J* = 10.6, 8.0, 1 H–C(4′)); 1.53 (*d*, *J* = 6.2, Me). ^{13}C-NMR: 139.2 (*s*, C(7a)); 138.7 (*s*, C(3a)); 129.5 (*d*, C(5)); 128.1 (*d*, C(6)); 125.2 (*s*, C(1)); 123.4 (*d*, C(7)); 120.9 (*d*, C(4)); 81.2 (*d*, C(5′)); 71.6 (*t*, C(3)); 40.3 (*t*, C(4′)); 20.3 (*q*, Me). ESI-MS (MeOH + NaI): 439 (5, $[2M+Na]^+$), 231 (100, $[M + Na]^+$), 157 (17). Anal. calc. for $C_{11}H_{12}O_2S$ (208.28): C 63.43, H 5.81, S 15.40; found: C 63.43, H 5.89, S 15.46.

3.2. *With (*R*)-2-Phenyloxirane* (**6**). Reaction of **1** (150 mg, 1 mmol) with **6** (180 mg, 1.5 mmol) and 4.5 g of SiO_2 at r.t., 10 h, and CC (Alox, hexane/Et_2O 10:1) yielded 79 mg (29%) of *(1*S*,4′*S*)-4′-Phenylspiro[1,3-dihydroisobenzofuran-1,2′-[1,3]oxathiolane]* (**7**), 26 mg (10%) of *(1*R*,4′*S*)-4′-phenylspiro[1,3-dihydroisobenzofuran-1,2′-[1,3]oxathiolane]* (**8**). Repetition of the reaction of **1** (150 mg, 1 mmol) with **6** (180 mg, 1.5 mmol) for 10 h yielded 28% of **7**, 16% of **8**, and 29% of **5** based on ^{1}H-NMR analysis of the reaction mixture and a weighed amount of 1,1,2,2-tetrachloroethane. In addition, 26% of **1** remained (*Scheme 3*).

Data of **7**: Colorless crystals. M.p. 112.5 – 113.4 °. $[\alpha]_D^{23}$ = – 63.9 (> 99% ee). IR (KBr): 3050*w*, 3028*w*, 2981*w*, 2942*m*, 2886*w*, 2874*m*, 1601*w*, 1495*m*, 1475*w*, 1462*s*, 1351*m*, 1303*w*, 1283*s*, 1251*s*, 1236*s*, 1197*m*, 1147*m*, 1108*s*, 1085*m*, 1054v*s*, 1018v*s*, 1007v*s*, 984*s*, 962v*s*, 947v*s*, 938v*s*, 929v*s*, 874*w*, 795*w*, 766v*s*, 752*s*, 702*s*. ^{1}H-NMR: 7.57 (*d*, *J* = 6.9, H–C(7)); 7.53 (*d*, *J* = 7.4, 2 arom. H of Ph); 7.41–7.36 (*m*, H–C(5), 2 arom. H of Ph, H–C(6)); 7.31–7.28 (*m*, 1 arom. H of Ph); 7.26–7.24 (*m*, H–C(4)); 5.19 (*d*, *J* = 12.6, 1 H–C(3)); 5.13 (*d*, *J* = 12.6, 1 H–C(3)); 4.95 (*dd*, *J* = 5.9, 2.2, H–C(4′)); 4.68 (*dd*, *J* = 9.4, 5.9, 1 H–C(5′)); 4.51 (*dd*, *J* = 9.3, 2.3, 1 H–C(5′)). ^{13}C-NMR: 142.5 (*s*, 1 arom. C of Ph); 139.6 (*s*, C(7a)); 137.5 (*s*, C(3a)); 130.0 (*d*, C(5)); 129.0 (*d*, 2 arom. CH of Ph); 128.4 (*d*, C(6)); 127.8 (*d*, 1 arom. CH of Ph); 127.4 (*d*, 2 arom. CH of Ph); 125.8 (*s*, C(1)); 124.2 (*d*, C(7)); 121.1 (*d*, C(4)); 77.0 (*t*, C(5′)); 72.2 (*t*, C(3)); 54.2 (*d*, C(4′)). CI-

MS (NH_3): 271 (1, $[M + H]^+$), 153 (9), 152 (100). Anal. calc. for $C_{16}H_{14}O_2S$ (270.35): C 71.08, H 5.22, S 11.86; found: C 70.92, H 5.03, S 11.63.

Crystals of **7** suitable for the X-ray crystal-structure determination were grown from Et_2O/hexane.

Data of **8**: Colorless crystals. M.p. 120.4 – 124.0 . $[\alpha]_D^{23}$ = + 61.2 (> 99% ee). IR (KBr): 3079*w*, 3061*w*, 3029*w*, 2978*w*, 2940*w*, 2923*w*, 2879*w*, 1600*w*, 1492*w*, 1461*m*, 1454*w*, 1367*w*, 1354*w*, 1281*w*, 1257*m*, 1242*m*, 1200*w*, 1189*w*, 1110*m*, 1082*w*, 1061*s*, 1047*m*, 1009*s*, 992*s*, 973*m*, 949*s*, 927*m*, 859*w*, 755*s*, 726*w*, 698*s*. ^{1}H-NMR: 7.59–7.58 (*m*, H–C(7), 2 arom. H of Ph); 7.42–7.39 (*m*, H–C(5), H–C(6)); 7.37–7.35 (*m*, 2 arom. H of Ph); 7.31–7.28 (*m*, 1 arom. H of Ph); 7.27–7.24 (*m*, H–C(4)); 5.21 (*d*, *J* = 12.6, 1 H–C(3)); 5.19 (*d*, *J* = 12.6, 1 H–C(3)); 5.08 (*dd*, *J* = 10.4, 6.4, H–C(4′)); 4.56 (*dd*, *J* = 9.3, 6.4, 1 H–C(5′)); 4.26 (*dd*, *J* = 10.3, 9.5, 1 H–C(5′)). ^{13}C-NMR: 139.5 (*s*, C(7a)); 137.8 (*s*, C(3a)); 137.1 (*s*, 1 arom. C of Ph); 130.0 (*d*, C(5)); 129.0 (*d*, 2 arom. CH of Ph); 128.6 (*d*, 2 arom. CH of Ph); 128.4 (*d*, C(6)); 128.2 (*d*, 1 arom. CH of Ph); 126.0 (*s*, C(1)); 124.2 (*d*, C(4)); 121.0 (*d*, C(7)); 77.0 (*t*, C(5′)); 72.4 (*t*, C(3)); 56.6 (*d*, C(4′)). CI-MS (NH_3): 271 (1, $[M + H]^+$), 153 (9), 152 (100). Anal. calc. for $C_{16}H_{14}O_2S$ (270.35): C 71.08, H 5.22, S 11.86; found: C 71.00, H 5.02, S 11.78.

Crystals of **8** suitable for the X-ray crystal-structure determination were grown from Et_2O/hexane.

4. Reactions of **9**. 4.1. *With (*S*)-2-Methyloxirane* (**2**). Reaction of **9** (328 mg, 2 mmol) with **2** (232 mg, 4 mmol) and 4.5 g of SiO_2 at r.t., 3 d; CC (SiO_2, hexane/AcOEt 10:1) yielded 180 mg (40%) of a mixture of *(2*S*,5′*S*)-5′-methylspiro[chroman-2,2′-[1,3]oxathiolane]* (**10**) and *(2*R*,5′*S*)-5′-methylspiro[chroman-2,2′-[1,3]oxathiolane]* (**11**). The ^{1}H-NMR spectrum of the mixture showed 32% of **10** and 8% of **11**. Separation of the two diastereoisomers by HPLC (*Nucleosil 100-7* column, hexane/THF 125:1) gave 130 mg (29%) of **10**, but **11** could not be purified due to its partial epimerization to **10** (*Scheme 4*).

Data of **10**: Colorless crystals. M.p. 69.0–70.1 . $[\alpha]_D^{23}$= + 217.4 (> 99% ee). IR (KBr): 3075*w*, 3053*w*, 3038*w*, 2989*w*, 2979*w*, 2966*m*, 2921*m*, 2851*w*, 1607*w*, 1580*m*, 1487*s*, 1457*m*, 1445*m*, 1379*w*, 1352*w*, 1345*w*, 1324*w*, 1299*w*, 1275*w*, 1234*s*, 1201*s*, 1174*w*, 1160*m*, 1138*s*, 1108*w*, 1087*m*, 1067*s*, 1049*s*, 1021*m*, 992*s*, 972*w*, 939*m*, 921*w*, 893*s*, 880*s*, 863*m*, 852*m*, 838*m*, 758*s*. ^{1}H-NMR: 7.12–7.09 (*m*, H–C(7)); 7.08 (*d*, *J* = 7.6, H–C(5)); 6.89 (*td*, *J* = 7.4, 1.1, H–C(6)); 6.83 (*dd*, *J* = 8.2, 0.8, H–C(8)); 4.83–4.78 (*m*, H–C(5′)); 3.29 (*dd*, *J* = 10.0, 4.9, 1 H–C(4′)); 3.09–3.03 (*m*, 1 H–C(4)); 2.91–2.86 (*m*, 1 H–C(4)); 2.87 (*t*, *J* = 10.0, 1 H–C(4′)); 2.43–2.39 (*m*, 1 H–C(3)); 2.35–2.30 (*m*, 1 H–C(3)); 1.45 (*d*, *J* = 6.1, Me). ^{13}C-NMR: 152.8 (*s*, C(8a)); 129.0 (*d*, C(5)); 127.4 (*d*, C(7)); 121.3 (*s*, C(4a)); 121.2 (*d*, C(6)); 117.3 (*d*, C(8)); 116.2 (*s*, C(2)); 79.0 (*d*, C(5′)); 39.6 (*t*, C(4′)); 33.3 (*t*, C(3)); 24.2 (*t*, C(4)); 18.9 (*q*, Me). EI-MS: 222 (21, $M^{+\bullet}$), 149 (11), 148 (100), 120 (43), 91 (12), 74 (11). Anal. calc. for $C_{12}H_{14}O_2S$ (222.31): C 64.83, H 6.35, S 14.42; found: C 64.96, H 6.59, S 14.59.

Crystals of **10** suitable for the X-ray crystal-structure determination were grown from Et_2O/MeOH.

Data of **11**: ^{1}H-NMR (300 MHz): 4.71–4.58 (*m*, H–C(5′)); 1.55 (*d*, *J* = 6.1, Me); the other signals at 7.12–7.07, 6.90–6.80, 3.32–2.85; 2.48–2.29 overlap with those of **10**.

4.2. *With (*R*)-2-Phenyloxirane* (**6**). Reaction of **9** (328 mg, 2 mmol) with **6** (360 mg, 3 mmol) and 4.5 g of SiO_2 at r.t., 3 d, CC (SiO_2, hexane/Et_2O 10:1), and HPLC (*Nucleosil 100-7* column, hexane/t-BuOMe 150:1) yielded 200 mg (35%) of *(2*R*,4′*S*)-4′-phenylspiro[chroman-2,2′-[1,3]oxathiolane]* (**12**) and 38 mg (7%) of *(2*S*,4′*S*)-4′-phenylspiro[chroman-2,2′-[1,3]oxathiolane]* (**13**) (*Scheme 5*).

Data of **12**: Colorless crystals. M.p. 63.4 – 65.8 . $[\alpha]_D^{23}$= – 154.6 (89% ee). IR (KBr): 3081*w*, 3061*w*, 3028*w*, 2975*w*, 2942*m*, 2884*w*, 2844*w*, 1608*w*, 1600*w*, 1581*s*, 1487*s*, 1454*s*, 1440*m*, 1429*m*, 1347*m*, 1332*w*, 1303*m*, 1272*m*, 1235*s*, 1209*s*, 1145*s*, 1108*s*, 1068*s*, 1035*s*, 1013*m*, 987*s*, 938*s*, 911*s*, 895*s*, 880*s*, 861*m*,

836*s*, 794*w*, 757*s*, 742*m*, 697*s*. ^{1}H-NMR: 7.40–7.39 (*m*, 2 arom. H of Ph); 7.33–7.31 (*m*, 2 arom. H of Ph); 7.27–7.24 (*m*, 1 arom. H of Ph); 7.14–7.11 (*m*, H–C(7)); 7.09 (*d*, *J* = 7.5, H–C(5)); 6.91 (*td*, *J* = 7.4, 1.1, H–C(6)); 6.88 (*dd*, *J* = 8.2, 0.9, H–C(8)); 4.86 (*dd*, *J* = 5.9, 1.9, H–C(4′)); 4.78 (*dd*, *J* = 9.3, 6.0, 1 H–C(5′)); 4.40 (*dd*, *J* = 9.2, 2.0, 1 H–C(5′)); 3.15–3.10 (*m*, 1 H–C(4)); 2.94–2.89 (*m*, 1 H–C(4)); 2.60–2.55 (*m*, 1 H–C(3)); 2.51–2.46 (*m*, 1 H–C(3)). ^{13}C-NMR: 152.9 (*s*, C(8a)); 142.4 (*s*, 1 arom. C of Ph); 129.2 (*d*, C(5)); 128.9 (*d*, 2 arom. CH of Ph); 127.8 (*d*, 1 arom. CH of Ph); 127.7 (*d*, C(7)); 127.4 (*d*, 2 arom. CH of Ph); 121.7 (*d*, C(6)); 121.4 (*s*, C(4a)); 118.1 (*s*, C(2)); 117.5 (*d*, C(8)); 77.6 (*t*, C(5′)); 53.2 (*d*, C(4′)); 33.0 (*t*, C(3)); 24.4 (*t*, C(4)). EI-MS: 284 (7, $M^{+\bullet}$), 149 (11), 148 (100), 137 (10), 136 (79), 135 (52), 120 (69), 119 (14), 105 (10), 104 (99), 103 (45), 92 (11), 91 (52), 78 (48), 77 (24). Anal. calc. for $C_{17}H_{16}O_2S$ (284.37): C 71.80, H 5.67, S 11.28; found: C 72.07, H 5.88, S 11.06.

Data of **13**: Colorless oil. $[\alpha]_D^{23}$ = + 44.4 (90% ee). IR (film): 3062*w*, 3028*w*, 2972*w*, 2936*w*, 2847*w*, 1601*w*, 1583*m*, 1489*s*, 1455*s*, 1349*w*, 1302*w*, 1274*w*, 1236*m*, 1211*s*, 1195*s*, 1156*w*, 1110*s*, 1070*m*, 1052*s*, 1038*s*, 1026*s*, 988*s*, 937*w*, 914*m*, 893*m*, 880*s*, 858*w*, 837*w*, 758*s*, 700*s*. ^{1}H-NMR: 7.53 (*d*, *J* = 7.3, 2 arom. H of Ph); 7.35 (*t*-like, *J* ≈ 7.6, 2 arom. H of Ph); 7.28 (*t*-like, *J* ≈ 7.6, 1 arom. H of Ph); 7.16–7.14 (*m*, H–C(7)); 7.10 (*d*, *J* = 7.5, H–C(5)); 6.95–6.91 (*m*, H–C(8), H–C(6)); 4.94 (*dd*, *J* = 10.4, 6.6, H–C(4′)); 4.54 (*dd*, *J* = 9.4, 6.7, 1 H–C(5′)); 4.36 (*dd*, *J* = 10.3, 9.5, 1 H–C(5′)); 3.10–3.07 (*m*, 1 H–C(4)); 2.93–2.89 (*m*, 1 H–C(4)); 2.51–2.40 (*m*, 2 H–C(3)). ^{13}C-NMR: 152.9 (*s*, C(8a)); 137.3 (*s*, 1 arom. C of Ph); 129.3 (*d*, C(5)); 128.9 (*d*, 2 arom. CH of Ph); 128.7 (*d*, 2 arom. CH of Ph); 128.2 (*d*, 1 arom. CH of Ph); 127.7 (*d*, C(7)); 121.7 (*d*, C(6)); 121.5 (*s*, C(4a)); 118.2 (*s*, C(2)); 117.6 (*d*, C(8)); 77.3 (*t*, C(5′)); 55.0 (*d*, C(4′)); 33.2 (*t*, C(3)); 24.2 (*t*, C(4)). EI-MS: 284 (14, $M^{+\bullet}$), 149 (11), 148 (97), 137 (11), 136 (91), 135 (47), 120 (56), 119 (11), 105 (11), 104 (100), 103 (39), 91 (36), 78 (33), 77 (16).

5. Reactions of **14**. 5.1. *With (*S*)-2-Methyloxirane* (**2**). Reaction of **14** (232 mg, 2 mmol) with **2** (232 mg, 4 mmol) and 4.5 g of SiO_2 at 0°, 2 d; CC (SiO_2, hexane/Et_2O/Et_3N 10:1:0.1) yielded 230 mg (66%) of a mixture of *(2*S*,5*R*)-2-methyl-1,6-dioxa-4-thiaspiro[4.5]decane* (**15**) and *(2*S*,5*S*)-2-methyl-1,6-dioxa-4-thiaspiro[4.5]decane* (**16**). Separation of the two diastereoisomers by MPLC (SiO_2, hexane/AcOEt 15:1) gave 100 mg (29%) of **15**. Further purification by HPLC (*Nucleosil 100-7* column, hexane/AcOEt/Et_3N 45:1:0.05) yielded 30 mg (9%) of **15,** but **16** was obtained only in 90% purity because of its partial epimerization to **15**. Repetition of the reaction of **14** (116 mg, 1 mmol) with **2** (116 mg, 2 mmol) at 0°, 2 d yielded 63% of **15**, 22% of **16**, and 15% of *tetrahydropyran-2-one* (**17**) according to the ^{1}H-NMR analysis of the reaction mixture and 1,1,2,2-tetrachloroethane as a standard (*Scheme 6*).

Data of **15**: Colorless oil. $[\alpha]_D^{23}$ = + 202.1 (> 99% ee). IR (film): 2963*s*, 2937*s*, 2862*s*, 1465*m*, 1452*m*, 1440*m*, 1381*m*, 1354*m*, 1282*m*, 1256*w*, 1230*w*, 1211*m*, 1185*s*, 1165*m*, 1147*s*, 1115*m*, 1092*m*, 1075*s*, 1037*s*, 1021*s*, 975*m*, 940*m*, 925*w*, 899*m*, 871*m*, 856*m*, 813*m*, 756*w*. ^{1}H-NMR: 4.65–4.59 (*m*, H–C(2)); 3.94–3.90 (*m*, 1 H–C(7)); 3.78–3.74 (*m*, 1 H–C(7)); 3.11 (*dd*, *J* = 9.9, 5.0, 1 H–C(3)); 2.76 (*t*, *J* = 10.0, 1 H–C(3)); 2.08–1.98 (*m*, 2 H–C(10)); 1.94–1.88 (*m*, 1 H–C(9)); 1.66–1.60 (*m*, 1 H–C(9)); 1.58–1.52 (*m*, 2 H–C(8)); 1.44 (*d*, *J* = 6.2, Me). ^{13}C-NMR: 118.1 (*s*, C(5)); 78.3 (*d*, C(2)); 65.1 (*t*, C(7)); 39.0 (*t*, C(3)); 37.4 (*t*, C(10)); 24.7 (*t*, C(8)); 22.5 (*t*, C(9)); 19.2 (*q*, Me). CI-MS (NH_3): 177 (5), 176 (10), 175 (100, $[M + H]^+$), 118 (39). Anal. calc. for $C_8H_{14}O_2S$ (174.26): C 55.14, H 8.10, S 18.40; found: C 55.25, H 8.25, S 18.30.

Data of **16**: Colorless oil. $[\alpha]_D^{23}$ = – 136.8 (> 99% ee) (containing 10% of **15**). ^{1}H-NMR (C_6D_6): 4.33–4.28 (*m*, H–C(2)); 3.83–3.73 (*m*, 2 H–C(7)); 2.71–2.65 (*m*, 2 H–C(3)); 2.11–2.01 (*m*, 2 H–C(10)); 1.62–1.56 (*m*, 1 H–C(9)); 1.44–1.37 (*m*, 1 H–C(9)); 1.24–1.18 (*m*, 1 H–C(8)); 1.23 (*d*, *J* = 6.2, Me); 1.14–1.09 (*m*, 1 H–C(8)). ^{13}C-NMR (C_6D_6): 120.5 (*s*, C(5)); 81.8 (*d*, C(2)); 66.1 (*t*, C(7)); 38.4 (*t*,

C(3)); 38.2 (*t*, C(10)); 25.4 (*t*, C(8)); 23.2 (*t*, C(9)); 21.7 (*q*, Me). CI-MS (NH_3): 176 (9), 175 (100, $[M + H]^+$), 118 (21).

5.2. *With (*R*)-2-Phenyloxirane* (**6**). Reaction of **14** (232 mg, 2 mmol) with **6** (360 mg, 3 mmol) and 4.5 g of SiO_2 at r.t., 11 h, CC (SiO_2, hexane/Et_2O/Et_3N 10:1:0.1), and MPLC (SiO_2, hexane/Et_2O 20:1) yielded 257 mg (54%) of *(3*S*,5*S*)-3-phenyl-1,6-dioxa-4-thiaspiro[4.5]decane* (**18**), 50 mg (11%) of *(3*S*,5*R*)-3-phenyl-1,6-dioxa-4-thiaspiro[4.5]decane* (**19**), and 36 mg (8%) of *(2*R*,5*R*)-2-phenyl-1,6-dioxa-4-thiaspiro[4.5]decane* (**20**) (*Scheme 7*).

Data of **18**: Colorless crystals. M.p. 49.3 – 51.4 °. $[\alpha]_D^{23}$ = – 168.7 (95% ee). IR (KBr): 3071*w*, 3028*w*, 3006*w*, 2962*s*, 2940*s*, 2924*s*, 2878*s*, 2846*m*, 1602*w*, 1494*m*, 1456*s*, 1437*m*, 1378*w*, 1363*w*, 1352*s*, 1342*m*, 1305*w*, 1286*m*, 1278*s*, 1263*m*, 1245*w*, 1203*s*, 1186*s*, 1171*m*, 1148*s*, 1129*s*, 1077*w*, 1061*s*, 1048*s*, 1016*s*, 959*s*, 942*s*, 930*s*, 898*s*, 868*s*, 846*w*, 834*m*, 820*m*, 802*w*, 763*s*, 698*s*. ^{1}H-NMR: 7.38–7.36 (*m*, 2 arom. H); 7.31–7.28 (*m*, 2 arom. H); 7.24–7.22 (*m*, 1 arom. H); 4.65 (*dd*, *J* = 6.1, 1.5, H–C(3)); 4.62 (*dd*, *J* = 9.0, 6.0, 1 H–C(2)); 4.33 (*dd*, *J* = 9.0, 1.7, 1 H–C(2)); 3.98–3.94 (*m*, 1 H–C(7)); 3.83–3.79 (*m*, 1 H–C(7)); 2.27–2.23 (*m*, 1 H–C(10)); 2.20–2.16 (*m*, 1 H–C(10)); 1.98–1.94 (*m*, 1 H–C(9)); 1.71–1.64 (*m*, 1 H–C(9)); 1.61–1.57 (*m*, 2 H–C(8)). ^{13}C-NMR: 143.0 (*s*, 1 arom. C); 128.6 (*d*, 2 arom. CH); 127.4 (*d*, 1 arom. CH); 127.2 (*d*, 2 arom. CH); 119.6 (*s*, C(5)); 76.9 (*t*, C(2)); 65.3 (*t*, C(7)); 52.3 (*d*, C(3)); 36.7 (*t*, C(10)); 24.6 (*t*, C(8)); 22.4 (*t*, C(9)). CI-MS (NH_3): 238 (11), 237 (76, $[M + H]^+$), 119 (6), 118 (100). Anal. calc. for $C_{13}H_{16}O_2S$ (236.33): C 66.07, H 6.82, S 13.57; found: C 66.06, H 6.85, S 13.35.

Data of **19**: Colorless crystals. M.p. 74.4 – 74.7 °. $[\alpha]_D^{23}$ = + 69.0 (90% ee). IR (KBr): 3074*w*, 3027*w*, 2968*w*, 2941*m*, 2880*w*, 2853*w*, 1600*w*, 1491*w*, 1453*w*, 1439*w*, 1377*w*, 1361*w*, 1351*w*, 1335*w*, 1282*w*, 1278*w*, 1263*w*, 1202*w*, 1189*w*, 1155*w*, 1130*m*, 1061*m*, 1055*m*, 1013*s*, 969*w*, 955*m*, 928*m*, 897*m*, 868*w*, 858*w*, 836*w*, 816*w*, 760*m*, 704*m*, 696*m*. ^{1}H-NMR: 7.46–7.44 (*m*, 2 arom. H); 7.33–7.30 (*m*, 2 arom. H); 7.27–7.24 (*m*, 1 arom. H); 4.84 (*dd*, *J* = 10.3, 6.8, H–C(3)); 4.51

(*dd*, *J* = 9.3, 6.7, 1 H–C(2)); 4.20 (*dd*, *J* = 10.3, 9.4, 1 H–C(2)); 4.05–4.01 (*m*, 1 H–C(7)); 3.92–3.88 (*m*, 1 H–C(7)); 2.17–2.13 (*m*, 1 H–C(10)); 2.09–2.05 (*m*, 1 H–C(10)); 1.96–1.91 (*m*, 1 H–C(9)); 1.69–1.57 (*m*, 1 H–C(9), 2 H–C(8)). ^{13}C-NMR: 138.0 (*s*, 1 arom. C); 128.6 (*d*, 2 arom. CH); 128.4 (*d*, 2 arom. CH); 127.8 (*d*, 1 arom. CH); 119.9 (*s*, C(5)); 76.7 (*t*, C(2)); 65.1 (*t*, C(7)); 54.1 (*d*, C(3)); 36.9 (*t*, C(10)); 24.6 (*t*, C(8)); 22.2 (*t*, C(9)). CI-MS (NH_3): 238 (14), 237 (100, $[M + H]^+$), 118 (70), 101 (6). Anal. calc. for $C_{13}H_{16}O_2S$ (236.33): C 66.07, H 6.82, S 13.57; found: C 65.96, H 7.01, S 13.49.

Crystals of **19** suitable for the X-ray crystal-structure determination were grown from Et_2O/hexane.

Data of **20**: Colorless crystals. M.p. 55.6 – 56.9 . $[\alpha]_D^{23}$ = – 21.0 (97% ee). IR (KBr): 3068*w*, 3025*w*, 2987*w*, 2968*w*, 2941*m*, 2924*m*, 2891*m*, 2857*m*, 1488*w*, 1462*w*, 1454*m*, 1441*w*, 1422*w*, 1385*w*, 1347*w*, 1325*w*, 1308*w*, 1290*w*, 1260*w*, 1215*m*, 1205*m*, 1184*s*, 1155*m*, 1126*m*, 1070*s*, 1035*s*, 1019v*s*, 1000*m*, 990*s*, 948*m*, 940*s*, 914*w*, 907*w*, 887*s*, 871*s*, 847*m*, 811*s*, 767*s*, 739*m*, 700*s*. ^{1}H-NMR: 7.47–7.45 (*m*, 2 arom. H); 7.36–7.34 (*m*, 2 arom. H); 7.31–7.28 (*m*, 1 arom. H); 5.30 (*dd*, *J* = 9.8, 6.1, H–C(2)); 4.06–4.02 (*m*, 1 H–C(7)); 3.96–3.91 (*m*, 1 H–C(7)); 3.24–3.19 (*m*, 2 H–C(3)); 2.17–2.08 (*m*, 2 H–C(10)); 1.95–1.91 (*m*, 1 H–C(9)); 1.66–1.56 (*m*, 1 H–C(9), 2 H–C(8)). ^{13}C-NMR: 139.9 (*s*, 1 arom. C); 128.7 (*d*, 2 arom. CH); 128.4 (*d*, 1 arom. CH); 126.8 (*d*, 2 arom. CH); 119.7 (*s*, C(5)); 87.6 (*d*, C(2)); 66.4 (*t*, C(7)); 39.1 (*t*, C(3)); 37.4 (*t*, C(10)); 24.9 (*t*, C(8)); 22.7 (*t*, C(9)). CI-MS (NH_3): 238 (8), 237 (49, $[M + H]^+$), 135 (13), 118 (100).

Crystals of **20** suitable for the X-ray crystal-structure determination were grown from Et_2O/MeOH.

6. *X-Ray Crystal-Structure Determination of* **3**, **7**, **8**, **10**, **19**, *and* **20** (*Table 1* and *Figs. 1 – 4*)[3]). All measurements were performed on a *Nonius KappaCCD* diffractometer [17] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream* 700 cooler. The data collection and refinement parameters are given in *Table 1*, and views of the molecules are shown in *Figs. 1 – 4*. Data reduction was performed with *HKL Denzo* and *Scalepack* [18]. The intensities were corrected for *Lorentz* and polarization effects, and an absorption correction based on the multi-scan method [19] was applied. The structures were solved by direct methods using SIR92 [20], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent C-atom (1.5 U_{eq} for the methyl group in **3** and **10**). The refinement of each structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied in the cases of **10**, **19**, and **20**. In **3,** one reflection, whose intensitiy was considered to be an extreme outliner, was omitted from the final refinement. Refinement of the absolute structure parameter [21] yielded values of – 0.1(2), – 0.04(6), 0.05(8), 0.03(7), 0.05(7), and 0.01(7) for **3**, **7**, **8**, **10**, **19**, and **20**, respectively, which confidently confirms that the refined coordinates represent the true enantiomorph in each case except for **3**, which, due to the low precision, does not give an unambiguous indication of the

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[3]) CCDC- 235086 – 235091 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax: + 44-(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

correct absolute configuration. Neutral atom scattering factors for non-H-atoms were taken from [22a], and the scattering factors for H-atoms were taken from [23]. Anomalous dispersion effects were included in F_c [24]; the values for f' and f'' were those of [22b]. The values of the mass attenuation coefficients are those of [22c]. All calculations were performed using the *SHELXL97* [25] program.

Table 1

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Legends:

Fig. 1. *ORTEP Plot* [11] *of the molecular structure of* **3** (arbitrary numbering of the atoms; displacement ellipsoids with 50% probability)

Fig. 2. *ORTEP Plots* [11] *of the molecular structures of* a) **7** and b) **8** (arbitrary numbering of the atoms; displacement ellipsoids with 50% probability)

Fig. 3. *ORTEP Plot* [11] *of the molecular structure* **10** (arbitrary numbering of the atoms; displacement ellipsoids with 50% probability)

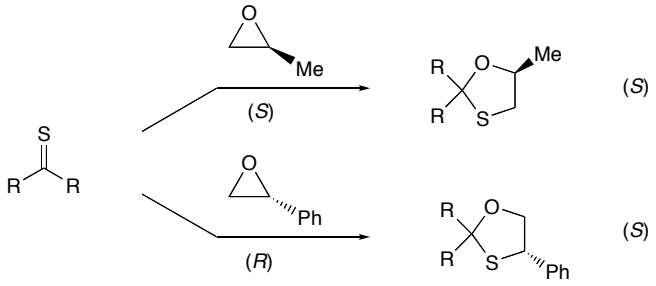
Fig. 4. *ORTEP Plots* [11] *of the molecular structures of* a) **19** and b) **20** (displacement ellipsoids with 50% probability)

Table 1. *Crystallographic Data of Compounds **3**, **7**, **8**, **10**, **19**, and **20***

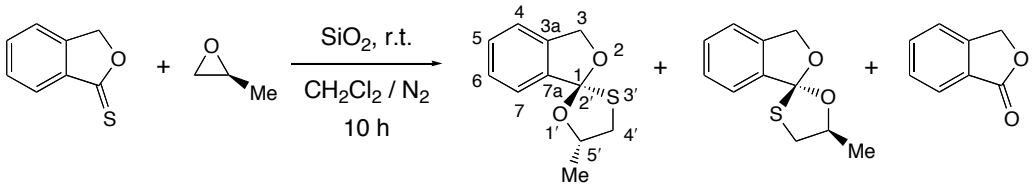
	3	**7**	**8**	**10**	**19**	**20**
Crystallized from	hexane/i-PrOH	Et_2O/hexane	Et_2O/hexane	Et_2O/MeOH	Et_2O/hexane	Et_2O/MeOH
Empirical formula	$C_{11}H_{12}O_2S$	$C_{16}H_{14}O_2S$	$C_{16}H_{14}O_2S$	$C_{12}H_{14}O_2S$	$C_{13}H_{16}O_2S$	$C_{13}H_{16}O_2S$
Formula weight [g mol^{-1}]	208.27	270.34	270.34	222.30	236.33	236.33
Crystal color, habit	colorless, prism	colorless, prism	colorless, tablet	colorless, plate	colorless, prism	colorless, plate
Crystal dimensions [mm]	0.05 × 0.18 × 0.20	0.22 × 0.22 × 0.30	0.07 × 0.20 × 0.27	0.05 × 0.22 × 0.22	0.07 × 0.10 × 0.25	0.03 × 0.20 × 0.25
Temp. [K]	160(1)	160(1)	160(1)	160(1)	160(1)	160(1)
Crystal system	tetragonal	orthorhombic	orthorhombic	orthorhombic	monoclinic	orthorhombic
Space group	$P4_12_12$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_1$	$P2_12_12_1$
Z	8	4	4	4	2	4
Reflections for cell determination	99506	26146	41579	17073	13314	25172
2θ range for cell determination [°]	4 – 50	4 – 60	4 – 60	4 – 60	4 – 55	4 – 60
Unit cell parameters a [Å]	7.7158(2)	5.6804(1)	5.9913(1)	6.1354 (1)	5.7737(2)	6.3724(1)
b [Å]	7.7158(2)	8.7193(1)	8.5129(2)	9.0937(2)	8.0009(3)	8.8038(2)
c [Å]	35.570(1)	26.6341(4)	26.1203(7)	19.1904(4)	12.9450(5)	21.2774(5)
β [°]	90	90	90	90	96.369(2)	90
V [Å^3]	2117.6(1)	1319.16(3)	1332.22(5)	1070.70(4)	594.30(4)	1193.69(4)
D_X [g cm^{-3}]	1.306	1.361	1.348	1.379	1.321	1.315
μ(MoK_α) [mm^{-1}]	0.276	0.239	0.237	0.278	0.254	0.253
Transmission factors (min; max)	0.736; 0.990	0.885; 0.956	0.912; 0.985	0.913; 0.988	0.888; 0.983	0.910; 0.994
$2\theta_{max}$ [°]	50	60	60	60	55	60
Total reflections measured	18451	24740	18535	21972	13745	21842
Symmetry-independent reflections	1865	3841	3877	3124	2617	3487
Reflections with $I > 2\sigma(I)$	1464	3236	2581	2806	2383	2832
Reflections used in refinement	1864	3841	3877	3124	2617	3487
Parameters refined	128	172	173	139	146	147
$R(F)$ [$I > 2\sigma(I)$ reflections]	0.0538	0.0353	0.0472	0.0322	0.0340	0.0369
$wR(F^2)$ (all data)	0.1089	0.0828	0.1064	0.0791	0.0778	0.0817
Weighting parameters [a; b][a])	0.0319; 2.4034	0.0351; 0.2187	0.049; 0.0	0.0371; 0.2533	0.0313; 0.183	0.0334; 0.2229
Goodness-of-fit	1.190	1.048	1.019	1.048	1.039	1.047
Secondary extinction coefficient	–	–	–	0.014(3)	0.048(7)	0.008(2)
Final Δ_{max}/σ	0.001	0.001	0.001	0.002	0.001	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.28; – 0.25	0.19; – 0.20	0.26; – 0.27	0.26; – 0.29	0.17; – 0.18	0.22; – 0.19

[a]) $w = [\sigma^2(F_o^2) + (aP)^2 + bP]^{-1}$, where $P = (F_o^2+2F_c^2)/3$

Scheme 1



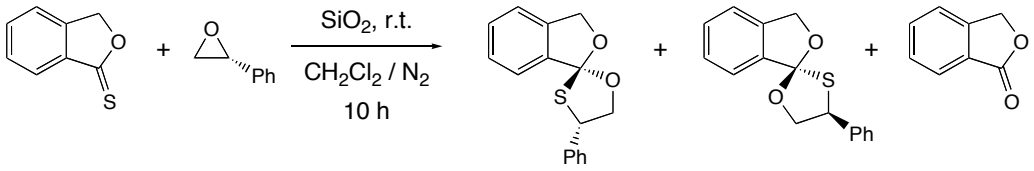
Scheme 2



1 **2** **3** **4** **5**

26% (> 99% ee) 10% (> 99% ee) 54%

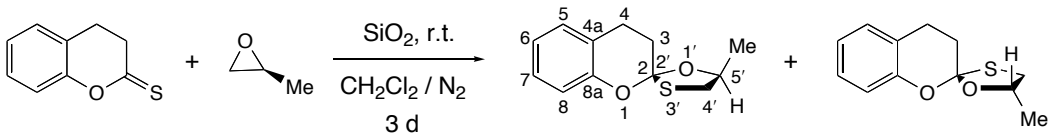
Scheme 3



1 **6** **7** **8** **5**

29% (> 99% ee) 16% (> 99% ee) 29%

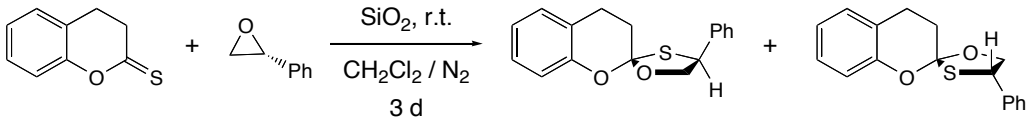
Scheme 4



9 **2** **10** **11**

32% (> 99% ee) 8%

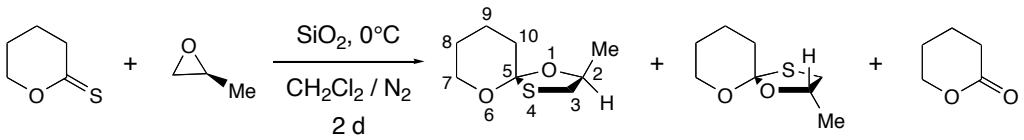
Scheme 5



9 **6** **12** **13**

35% (89% ee) 7% (90% ee)

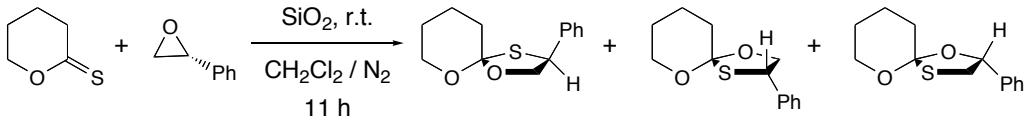
Scheme 6



14 **2** **15** **16** **17**

63% (> 99% ee) 22% 15%

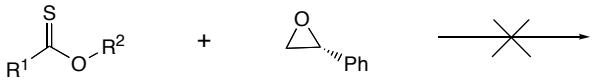
Scheme 7



14 **6** **18** **19** **20**

54% (95% ee) 11% (90% ee) 8% (97% ee)

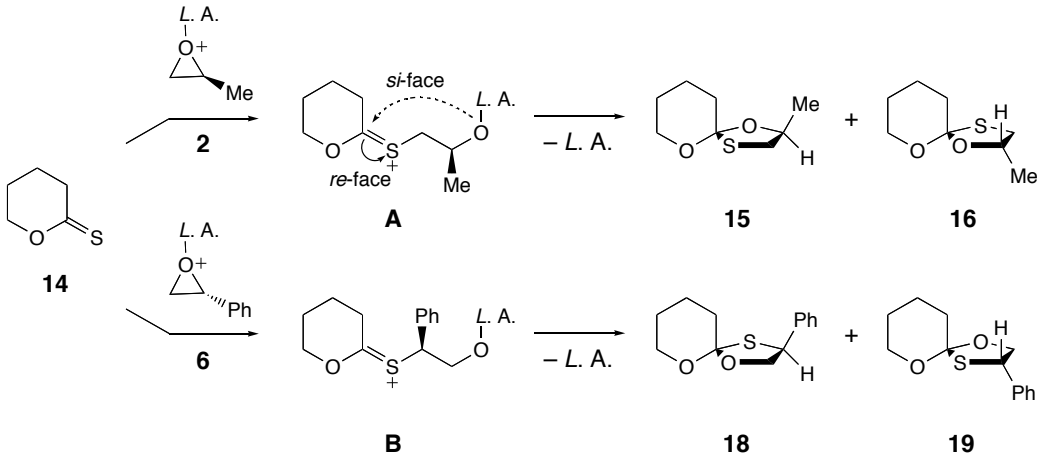
Scheme 8



21 **6**

21a R^1 = t-Bu, R^2 = Et
21b R^1 = Heptyl, R^2 = Me
21c R^1 = Ph, R^2 = Me
21d $R^1 = R^2$ = Ph

Scheme 9



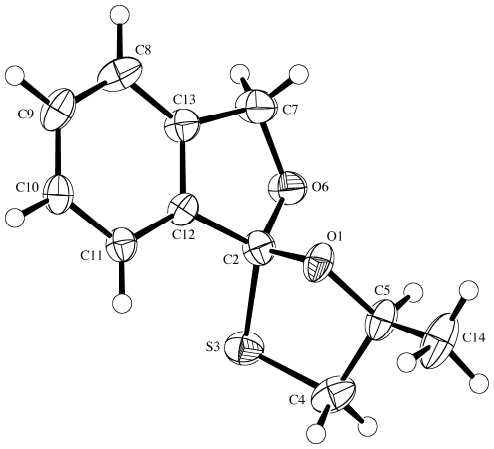
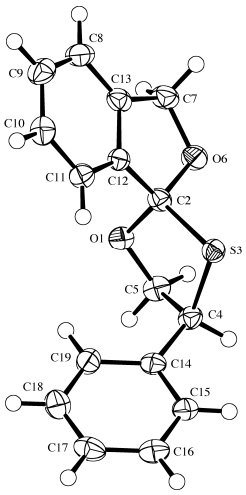


Fig. 1

a)


C8
C9
C13
C7
C10
O6
C11
C12
C2
O1
S3
C5
C4
C19
C14
C18
C15
C17
C16

b)

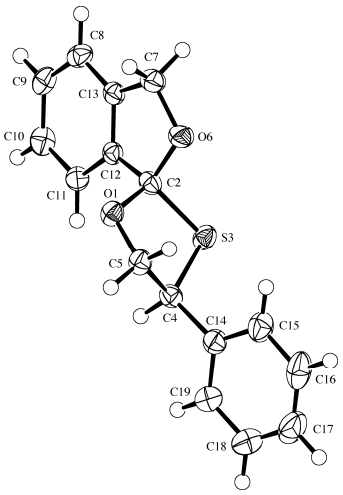

C8
C7
C9
C13
C10
O6
C12
C2
C11
O1
S3
C5
C4
C14
C15
C16
C19
C17
C18

Fig. 2

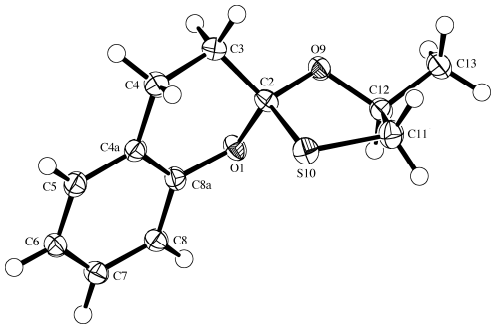
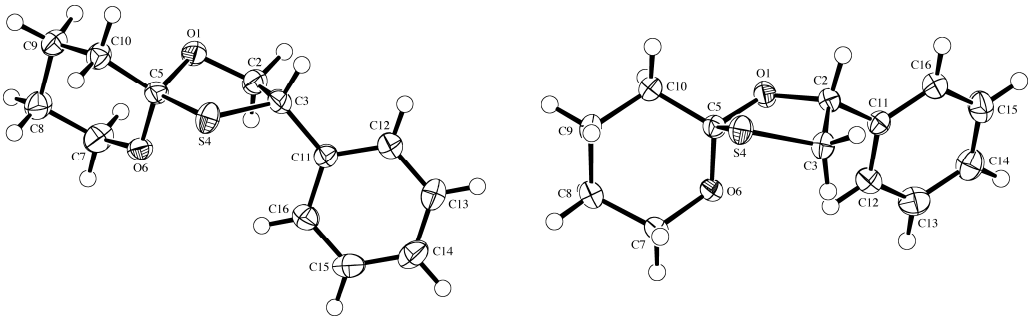


Fig.3

a) b)


C9
C10
O1
C5
C2
C3
C8
C7
O6
S4
C11
C12
C13
C16
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C10
O1
C2
C16
C5
C11
C15
C9
S4
C3
C14
C8
O6
C12
C7
C13

Fig. 4

Scheme Graphical Abstract